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PRINCIPAL INVESTIGATOR: Deborah L. Warden, M.D.

CONTRACTING ORGANIZATION: Walter Reed Army Medical Center
Washington, DC 20307

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Deborah L. Warden, M.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Walter Reed Army Medical Center
Washington, DC 20307

E-Mail: Deborah.warden@na.amedd.army.mil

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13. ABSTRACT (Maximum 200 Words)

Objectives: **1)** To examine the construct validity of the Automated Neuropsychological Metrics (ANAM), a computerized neuropsychological test battery. **2)** To compare TBI subjects to a comparable sample of controls to examine the effect of TBI and performance predictors and develop normative data.
Accomplishments/Issues: 1) Data analysis completed, manuscript written, and submitted to the Archives of Clinical Neuropsychology. The manuscript is undergoing peer review. This manuscript was attached to the final report from May 2004. **2)** This second analysis has now been completed and the manuscript written. This project was delayed secondary to the deployment of CDR Dennis Reeves (Ret.) to Iraq for 8 mos. in 2003. CDR Reeves collected much of the normative data needed and his expertise is critical for this analysis/manuscript preparation. The manuscript is currently under review by collaborating authors; will be submitted to a peer-reviewed journal, Applied Neuropsychology this summer (2005).
Results: 2.) Analyses of variance comparing ANAM performance between the TBI and control groups demonstrate that individuals with TBI show significantly slower mean reaction time on three of four ANAM tests despite generally similar accuracy rates. Results from the regression analyses demonstrated that injury severity (length of loss of consciousness), was the only significant predictor of ANAM performance.

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Traumatic brain injury, ANAM, computerized assessment, validity

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INTRODUCTION

There is a need for rapid and precise cognitive assessment in traumatic brain injury (TBI), particularly with milder injuries. Fast and accurate assessment would provide valuable information regarding whether or not an individual who has sustained an injury is ready to resume previous activities such as the playing field for athletes or the battlefield for soldiers (Warden, Bleiberg, Cameron, et al., 2001). Computerized neuropsychological measures, such as the Automated Neuropsychological Assessment Metrics (ANAM) have been developed with the goal of providing rapid and precise assessment of neurocognitive functioning (Kane & Reeves, 1997). However, the validity of such measures and the performance of patient populations compared to normal control subjects need to be demonstrated before clinical utility can be considered. The present project sought to: 1) examine the construct validity of the ANAM in relation to traditional neuropsychological measures; 2) compare TBI subjects to a comparable sample of USA controls to examine the effect of TBI and performance predictors and develop normative data.

BODY

TASK 1: DATA SETS

PLAN

To facilitate analyses, separate ANAM data sets including demographic (age, race, gender, education/service history), injury-related, neuropsychological, and psychiatric variables for the baseline and follow-up evaluations will be created. Study ID numbers will be used to identify subjects; no other personal identifiers will be used. The anticipated completion date for this data base portion is 2 months.

ACCOMPLISHMENTS/ISSUES

The data sets were created. There were no issues

TASK 2: CONSTRUCT VALIDITY

PLAN

The first planned analysis and paper will examine the construct validity of the ANAM in relation to traditional neuropsychological measures. Statistical analyses will include descriptives, correlational analysis, and factor analysis. While there are a number of studies examining the ANAM in a variety of populations, there has been very limited research regarding the construct validity of its tasks. Information regarding the factor structure of the ANAM and its relationship among its subtests and traditional neuropsychological measures is needed to validate the ANAM for clinical use. This analysis will examine the neuropsychological constructs measured by the ANAM and compare them with traditional neuropsychological measures assessing similar domains. It is hypothesized that the ANAM subtests will be related to the traditional neuropsychological measures purporting to tap similar areas of cognitive functioning.

ACCOMPLISHMENTS/ISSUES

Data analysis was completed and the manuscript was written and submitted to the Archives of Clinical Neuropsychology. The manuscript is currently undergoing peer review. This manuscript was attached to the original final report from May 2004.

TASK 3: NORMATIVE DATA AND TBI EFFECTS

PLAN

The second planned analysis and paper will compare our TBI subjects to a comparable sample of USA controls collected (e.g., Fort Bragg/USMC controls collected at Paris Island) to examine the effect of TBI and performance predictors and develop normative data. This will include factors such as injury severity (length of loss of consciousness, length of post traumatic amnesia). Statistical analyses will include descriptives, analysis of variance, and regression. As noted, the ANAM has been used in research with a number of populations, however, normative data for controls and specific clinical populations such as TBI are lacking. Also, among TBI patients, injury-related and premorbid factors affecting ANAM performance have not been examined. Therefore, these analyses will strive to examine the impact of TBI on ANAM performance and develop normative data for both TBI subjects and a similar group of non-injured control subjects. In general, it is hypothesized that positive TBI status will have a significant negative effect on ANAM performance. Moreover, it is believed that premorbid and injury related factors such as injury severity, prior TBI, etc. will be predictive of poorer ANAM

performance. The anticipated completion date for this second analysis and manuscript is 6 months following the completion of the first analysis and manuscript.

ACCOMPLISHMENTS/ISSUES

This analysis has now been completed and the manuscript written. A one year extension was given for completion of the analysis and manuscript. This project delay was the result of the deployment of CDR Dennis Reeves to Iraq as part of Operation Iraqi Freedom in spring 2003. CDR Reeves collected much of the normative data needed and this data in addition to his expertise was critical for this analysis and manuscript preparation. The manuscript is currently under review by collaborating authors; will be submitted to a peer-reviewed journal, Applied Neuropsychology this summer (2005).

KEY RESEARCH ACCOMPLISHMENTS

- Construct Validity Data Analysis (2004)
- Construct Validity Manuscript (2004)
- Normative Data and TBI Effects Analysis (2005)
- Normative Data and TBI Effects Manuscript (2005)

REPORTABLE OUTCOMES

- Construct Validity Manuscript (2004)
- Normative Data and TBI Effects Manuscript (2005)

CONCLUSIONS

Construct Validity Task: Our data demonstrate the construct validity of the ANAM in a sample of individuals with moderate to severe TBI. Specifically, correlational and factor analyses demonstrated some relationship between ANAM measures and tradition neuropsychological measures in TBI. However, there was no perfect overlap between ANAM measures and traditional measures. Rather it appears that the ANAM involves both cognitive constructs similar to traditional measures, as well as unique constructs. Certain ANAM measures involve the cognitive domains of attention/processing speed similar to more traditional neuropsychological measures. These measures, Memory Search and Running Memory, may be more useful when evaluating TBI patients. Future studies need to examine the ANAM in other patient populations. In particular, patients with more mild TBI's need to be examined, as it is this population that would most benefit from rapid cognitive screening to help inform return to play/work/duty decisions.

Normative Data and TBI Effects Task: Analyses of variance comparing ANAM performance between the TBI and control groups demonstrate that individuals with TBI show significantly slower mean reaction time on three of four ANAM tests despite generally similar accuracy rates. Results from the regression analyses demonstrated that injury severity (length of loss of consciousness), was the only significant predictor of ANAM performance. Our findings suggest that the ANAM is sensitive to the effects of relatively acute TBI and that severity of injury is the best predictor of ANAM test performance. Future studies are needed to examine patterns of recovery following TBI. Moreover, studies using the ANAM in older TBI and control populations, as well as in those with lower and higher levels of education are needed so that comprehensive normative data is available allowing for more wide spread use of this ANAM in cognitive assessment.

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APPENDIX 1: Normative Data and TBI Effects Manuscript

Running Head: ANAM Performance

Performance on the Automated Neuropsychological Metrics (ANAM) in Individuals with Moderate to Severe Traumatic Brain Injury Compared with Non-Injured Controls

Laurie M. Ryan,

Defense and Veterans Brain Injury Center, Walter Reed Army Medical Center, Washington DC,

Uniformed Services University of the Health Sciences, Bethesda, MD

Dennis L. Reeves,

Mental Health Department, Naval Hospital, Camp Pendleton, CA

Molly B. Sparling,

Defense and Veterans Brain Injury Center, Walter Reed Army Medical Center, Washington DC

Joseph Bleiberg,

Neuroscience Research, National Rehabilitation Hospital

Jack Spector,

University of Maryland, Baltimore, MD

Deborah L. Warden,

Defense and Veterans Brain Injury Center, Walter Reed Army Medical Center, Washington DC, Uniformed Services University of the Health Sciences, Bethesda, MD

Correspondence concerning this article should be addressed to Laurie M. Ryan, Defense and Veterans Brain Injury Center, Walter Reed Army Medical Center, PO Box 59181, Washington,

DC 20021. Telephone number: 202-782-6345. Fax number: 202-782-4400. E-mail:

laurie.ryan@na.amedd.army.mil; l.m.ryan@comcast.net

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Abstract

Primary Objective: The Automated Neuropsychological Metrics (ANAM) is a computerized neuropsychological test battery. The present study sought to examine ANAM performance in individuals with moderate to severe traumatic brain injury (TBI) compared to non-injured controls. Moreover, this study examined the impact of TBI on ANAM performance.

Design: Analysis of variance was conducted to compare ANAM performance between injured and non-injured individuals. Regression analysis was conducted to identify predictors of ANAM performance in injured individuals.

Methods: Participants were 140 active duty service members with moderate to severe traumatic brain injury (TBI) and 197 non-injured active duty Marine Corps recruits. All participants underwent ANAM testing.

Results: Analyses of variance comparing ANAM performance between the TBI and control groups demonstrate that individuals with TBI show significantly slower mean reaction time on three of four ANAM tests despite generally similar accuracy rates. Results from the regression analyses demonstrated that injury severity (length of loss of consciousness), was the only significant predictor of ANAM performance.

Conclusions: Our data demonstrate that the ANAM is sensitive to the effect of TBI.

Performance on the Automated Neuropsychological Metrics (ANAM) in Individuals with Moderate to Severe Traumatic Brain Injury Compared with Non-Injured Controls

There is a need for rapid and precise cognitive assessment in traumatic brain injury (TBI). Fast and accurate assessment would provide valuable information regarding whether or not an individual who has sustained an injury is ready to resume previous activities such as the playing field for athletes or the battlefield for soldiers.

The value of completing neuropsychological baseline and post injury assessments of athletes is gaining widespread acceptance in the medical community. Many college and professional sports teams are recognizing the need for concussion assessment and are utilizing computerized programs to use for rapid baseline and sideline assessments. Orientation, attention, memory and information processing are the basis of neuropsychological testing of an athlete. Neuropsychological examination provides an objective measure for the documentation of brain dysfunction when all other tests including physical and neurological examination are normal. As the effects of the concussion resolve, reliable improvement in performance on the neuropsychological battery occurs. The objective demonstration of cognitive and mental status abnormality is valuable for the athlete, parents, coaches, physicians and athletic trainers in understanding and following the extent of the injury. Results from high school, collegiate, and professional levels in many sports have affirmed the important role of this modality (Alves, Macciocchi, & Barth, 1993; Barrett, Ward, Boghey, Jones, & Mychalkin, 1994; Mittenberg, DiGiulio, Perrin, & Bass, 1992; Mittenberg 1994; Rimel, Giordani, Barth, Boll, & Jane, 1981).

A number of computerized cognitive assessments are available to follow individuals over time and guide return to play decisions. The Automated Neuropsychological Assessment

Metrics (ANAM; Kane & Reeves, 1997) was developed with the goal of providing rapid and precise assessment of neurocognitive functioning. The Defense and Veterans Brain Injury Center (DVBIC) has found the ANAM to be sensitive to concussion in studies of boxing students at the United States Military Academy at West Point (Warden, et al., 2001).

While computerized cognitive assessment serves a key role in the assessment of concussion, it may also be important for the evaluation of other types and severities of brain injury. However, data is limited regarding the effects of more severe TBI on ANAM performance. The present study sought to examine ANAM performance in individuals with moderate to severe TBI compared to a group of non-injured controls. In addition, the influence of TBI and demographic factors on ANAM performance was examined in the individuals with TBI.

Methods

Participants

The injured participants were 140 military health care beneficiaries, active duty service members, who sustained a moderate to severe TBI as demonstrated by admission Glasgow Coma Scale score of 13 or less, or 24 hours or more of posttraumatic amnesia, or focal cerebral contusion or hemorrhage on computed tomography or magnetic resonance imaging. Tables 1 and 2 provide demographic information and head injury status. All patients had recovered to a Ranchos Los Amigos level seven (oriented and cooperative) at the time of the evaluation. Patients were evaluated between one and three months post injury. The etiology of injury was predominantly from motor vehicle accidents. These participants were part of a randomized controlled treatment trial of rehabilitation (Salazar, et al., 2000). The non-injured controls were taken from a sample of 197 Marine Corps recruits (Gastaldo, Reeves, Levinson, & Winger,

2001). Table 3 provides demographic information for the controls. Comparison of demographic variables between the TBI individuals and the non-injured controls indicated significant difference for age and education ($p \leq .0005$). The TBI group is somewhat older (24.86 years compared to 19 years) with a larger range in age (18-47 years compared to 17-26 years). However, the modal age for the TBI group is only 21 years. The TBI group's education was only slightly higher (12.9 years compared to 12 years) but again the range was greater (11-21 years compared to 12-17 years). Finally, the percentage of females (7 or 5%) is significantly fewer in the TBI group than the percentage of females in the control group (83 or 42%). Given this large discrepancy in the percentage of females, only male control participants were included in the remaining analyses (n=114)

[Insert Tables 1, 2 and 3 About Here]

Materials and Procedures

All participants underwent ANAM testing. The ANAM measures included in both the TBI and control assessments included the following: Math Processing, Memory Search, Running Memory, and Spatial Processing (Levinson & Reeves, 1997). Math Processing (MP) involves simple calculations (addition and subtraction). Memory Search (MS) is an adaptation of the Sternberg technique (Sternberg, 1969) involving encoding, categorization, response selection and execution, and short-term memory. Running Memory (RM) involves continuous recall task involving encoding, storage, and working memory. Finally, Spatial Processing (SP) involves spatial orientation.

<u>Design and Analysis</u>

Analyses of variance were conducted to examine mean performance on ANAM measures for the TBI participants compared to the non-injured controls. Accuracy scores and reaction times scores were used for each ANAM test. Regression analyses were conducted to

examine the influence of injury and demographic factors on ANAM performance in the TBI participants. ANAM throughput scores were used in the regression analysis, as throughput is a measure of performance efficiency combining speed and accuracy.

Results

Results from the analyses of variance indicated some significant differences in performance on ANAM measures between the groups. See Tables 4 and 5 for mean ANAM scores by group. For the Running Memory (RM) test there was no significant difference regarding percent accuracy but mean reaction time was significantly slower in the TBI group ($F=25.71$, $p \leq .0005$). For the Mathematical Processing (MP) test, percent accuracy was slightly lower but statistically significant ($F=4.843$, $p \leq .029$) and once again mean reaction time was significantly slower ($F=13.91$, $p \leq .0007$). For the Memory Search (MS) test, the TBI group actually demonstrated slightly higher accuracy that was statistically significant ($F=8.40$, $p<.0045$) but again significantly slower mean reaction time ($F=244.90$, $p<.0005$). Finally, for the Spatial Processing (SP) test, the TBI demonstrated greater accuracy ($F=18.523$, $p \leq .00052$) but there were no significant differences for mean reaction time between the groups.

Multiple regression analyses were conducted to examine the influence of injury and demographic variables on ANAM performance for the TBI participants. The injury variables selected include severity of TBI based on length of loss of consciousness (LOC), the presence of frontal lesion(s) on magnetic resonance imaging (MRI), and prior history of head injury. LOC was dichotomized into one hour or less reflecting less severe injury and greater then one hour reflecting more severe injury (Salazar, et al., 2000). The presence or absence of a frontal lesion on MRI was chosen as frontal lesions can impact cognitive functioning such as attention and speed of processing which are tapped by the ANAM tests. Finally, TBI can have a cumulative

effect and prior history of injury may further negatively impact cognitive performance. Age and education can also affect cognitive performance (e.g. Lezak, 1995) and these demographic variables were included in the regression analyses. Gender can also affect cognitive performance but given the small number of female participants in the TBI sample this variable was not included in the regression analyses.

Results from the regression analyses yielded only one significant variable for most of the ANAM tests. Specifically, LOC was significant in the regression analyses for all ANAM tests except Mathematical Processing. None of the other variables included were significant.

[Insert Tables 4, 5 and 6 About Here]

Discussion

The findings from this study demonstrate that individuals with TBI show significantly slower mean reaction time across three of the four ANAM subtests despite generally similar accuracy rates. Slowed processing speed is a hallmark of TBI in milder and more severe injuries. These results suggest that ANAM measures, in particular the Running Memory, Mathematical Processing, and Memory Search, are sensitive to the relatively acute effects of TBI. While there were some minor differences in age and education between the groups, it is unlikely that these would account for the findings.

Results from the regression analyses demonstrated that injury severity, length of loss of consciousness, was the only significant predictor of performance across all but one ANAM test. Other injury and demographic factors including frontal lesions and prior history of TBI were not significant. Age and education were also not significant in the regression analyses. While age and education do influence cognitive functioning, it is generally the case that older age and lower

levels of education result in poorer performance. The current TBI sample is generally young and well educated and so this lack of significance is not surprising.

Our findings suggest that the ANAM is sensitive to the effects of relatively acute TBI and that severity of injury is the best predictor of ANAM test performance. Future studies are needed to examine patterns of recovery following TBI. Moreover, studies using the ANAM in older TBI and control populations, as well as in those with lower and higher levels of education are needed so that comprehensive normative data is available allowing for more wide spread use of this ANAM in cognitive assessment.

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Table 1

TBI Sample Demographics

N	140
Age	24.86 M ± 6.12 SD
Education (Years)	12.86 M ± 1.58 SD
Sex	Male: 133 Female: 7
Race	Caucasian: 97 African-American: 29
	Other: 14

Table 2

Head Injury Status

Cause of Injury	MVA: 77
	Blunt Object: 26
	Falls: 20
	Sports Related: 6
	Pedestrian: 5
	Other: 6
Length of Loss of Consciousness	< 1 hour: 52
	1-24 hours: 39
	>24 hours to 7 Days: 40
	>7 Days to 30 Days: 5
	Missing: 4
Length of Post Traumatic Amnesia	< 1 hour: 3
	1-24 hours: 18
	>24 hours to 7 Days: 60
	>7 Days to 30 Days: 55
	>30 Days: 2
	Missing: 12

Table 3

Control Sample Demographics

N	197	
Age	19 M $\pm$ 2.0 SD	
Education (Years)	12.0 M $\pm$ 1.0 SD	
Sex	Male: 114 Female: 83	
Race	Caucasian: 133	African-American: 38
	Other: 26	

Table 4

Mean ANAM Scores for the TBI Group

		Mean	Standard Deviation
RM			
	% Accuracy	92.6	9.0
	Mean Reaction Time	631.5	450.3
MP			
	% Accuracy	90.35	13.6
	Mean Reaction Time	3373	1381.5
MS			
	% Accuracy	93.5	7.2
	Mean Reaction Time	705.9	107.2
SP			
	% Accuracy	94.3	8.4
	Mean Reaction Time	2406.7	855.5

Table 5

Mean ANAM Scores for the Control Group

	Mean	Standard Deviation
RM		
% Accuracy	94	4.0
Mean Reaction Time	620	84.0
MP		
% Accuracy	93	8.0
Mean Reaction Time	2920	793.0
MS		
% Accuracy	91	8.0
Mean Reaction Time	1114	293.0
SP		
% Accuracy	90	9.0
Mean Reaction Time	2484	746.0

Table 6

Regression Coefficients for ANAM Measures for the TBI Group

	Variables	β	t	P value
RM	Age	.056	.481	.632
	Ed	-.069	-.611	.542
	Head Injury Hx	-.078	-.800	.425
	Frontal Lesion	.004	.038	.970
	LOC	-.192	-2.05	.042
MS	Age	.024	.210	.834
	Ed	-.099	-.870	.383
	Head Injury Hx	-.095	-.963	.338
	Frontal Lesion	-.031	-.326	.745
	LOC	-.204	-2.18	.032
SP	Age	-.154	-1.34	.183
	Ed	.160	1.43	.156
	Head Injury Hx	-.079	-.818	.415
	Frontal	.051	.549	.584
	LOC	-.186	-2.01	.047
MP	Age	-.054	-.458	.648
	Ed	-.020	-.174	.862
	Head Injury Hx	-.032	-.323	.747
	Frontal Lesion	-.063	-.657	.512
	LOC	-.138	-1.46	.148